REMARKS

Claims 1-90 are pending. Claims 31-90 have been withdrawn. Independent claims 1 and 16 have been amended. No new matter is believed to be added by these amendments. Claims 2-11, 13-15, 17-26, and 28-30 depend from claims 1 and 16, respectively.

In the present Office Action, claims 1-11, 13-26, and 28-30 are rejected under 35 U.S.C. §103(a) as being unpatentable over, "Combined Ultrasound and Fluorescence Spectroscopy for Physico-Chemical Imaging of Atherosclerosis" by Warren, *et al.* ("Warren") in view of Tomography – Definition from Dictionary.com. Claims 1-11, 13-26, and 28-30 are objected to for informality. Claims 1-11, 13-26, and 28-30 are rejected under 35 U.S.C. §112, first paragraph as failing to comply with the written description and enablement requirements. Applicants respectfully request allowance of all the pending claims in view of the subsequent remarks regarding the above-mentioned independent claims.

I. Claim Amendments

Independent claim 1 has been amended to further clarify that the claimed invention pertains to bioluminescence. Particularly claim 1 has been amended to clarify that the detecting and the producing steps are applied to bioluminescent signals, and not fluorescent signals. The claim now recites that "internally derived bioluminescent signals" are detected and further defines "internally derived bioluminescent signals" as "signals that are not reliant on external energy excitation." As has been discussed in earlier responses and is well known in the art, fluorescent signals require the use of an external energy excitation source to cause the emission of fluorescence, whereas bioluminescence is not reliant on any external energy source. Rather

bioluminescence is self generated by an organism. Support for this amendment can be found in the as filed application on page 1, line 14-20. Specifically:

> There are many "emission-detection" imaging techniques known in the art, such as bioluminescent imaging. However, such current imaging techniques are limited to the projective imaging mode or external excitation of the internal light source through external energy sources along selected paths. Therefore, three-dimensional structures and localization of an ***internally derived light source***, ***such as one not reliant on external energy excitation***, cannot be resolved with high quantitative accuracy both in terms of spatial location and localized activity.

(Emphasis added).

Claim 16 has been similarly amended and now recites that "internally derived bioluminescent signals" are detected and further defines "internally derived bioluminescent signals" as "signals that are not reliant on external energy excitation."

Claims 1 and 16 have also been amended to restructure the claim so as to positively recite an active method step and a structural limitation pertaining to producing the bioluminescent source distribution. Claims 1 and 16 have also been amended to ensure proper antecedent basis for "mapped optical properties." Claims 1 and 16 have both been amended to remove single/multi spectral radiative transfer equations and now recite "a radiative transfer equation or an approximation to the radiative transfer equation." No new matter is added by these amendments.

II. Claim Objections

Claims 1-11, 13-26, and 28-30 were objected to because it was unclear as to what structural limitation and active method step is set forth. Claims 1 and 16 have been amended to restructure the claims. Claim 1 now positively recites an active method step of producing the bioluminescent source distribution and claim 16 now positively recites that the bioluminescent

imaging device is configured for producing the bioluminescent source distribution. Thus, the claims now recite an active method step and structural limitation. Applicants respectfully request removal of the objection.

III. Rejections Under 35 U.S.C. §112, first paragraph

Claims 1-11, 13-26, and 28-30 were rejected 35 U.S.C. §112, first paragraph, for not complying with the written description and the enablement requirements. Specifically, the limitation of "single- or multi-spectral radiative transfer equation without an external excitation source term." While Applicants contend the specification as filed satisfies both the written description and enablement requirements, Applicants have amended claims 1 and 16 to remove the rejected limitation. Accordingly, Applicants respectfully request withdrawal of the rejection.

IV. Rejections Under 35 U.S.C. §103(a)

In the Office Action, claims 1-11, 13-26, and 28-30 were rejected under 35 U.S.C. §103(a) as unpatentable over Warren in view of Tomography – Definition from Dictionary.com. Applicants first submit that, for a *prima facie* case of obviousness, the cited prior art reference "must teach or suggest all the claim limitations" MPEP § 2143. Thus, if the reference does not teach each of the claimed limitations, a finding of obviousness fails. In addition, the Patent Office has the burden under § 103 to establish a *prima facie* case of obviousness, which can be satisfied only by showing some objective teaching in the prior art would lead one to combine the relevant teachings of the references. *See In re Fine*, 837 F.2d 1071, 1074 (Fed. Cir. 1988). As such, an Applicant, to overcome an allegation of obviousness, can show that the cited prior art references (when combined) do not teach or suggest all the claim limitations or that there is not an objective teaching in the prior art that would lead one to combine the relevant teachings of the references.

Independent claims 1 and 16 were rejected as being obvious in light of Warren in view of Tomography – Definition from Dictionary.com. However, Warren in view of Tomography – Definition from Dictionary.com fails to disclose, teach, or suggest at least the reconstruction of a bioluminescent source distribution. Applicants refer to their previous responses for the descriptions of the systems taught by Warren and Tomography – Definition from Dictionary.com. Applicants endeavor by this amendment to clarify that the claims are directed to bioluminescence and not fluorescence.

The claims as amended state that "internally derived bioluminescent signals" are detected with "a bioluminescent imaging device." Furthermore, the claims as amended state that "internally derived bioluminescent signals are not reliant on external energy excitation." The specification is clear that there is a difference between bioluminescence and fluorescence. The knowledge of one of skill in the art is clear that there is a difference between bioluminescence and fluorescence. One of those differences is the absolute requirement that fluorescence utilize an external excitation source. To reconstruct a fluorescent image, the interference created by the external light source to excite the fluorescent source and the process of fluorescent light being directed toward the external detectors have to be taken into account. In contrast, bioluminescence imaging is not complicated by the fluorescence issues. Hence, bioluminescence imaging has a much better signal to noise ratio or sensitivity than fluorescent imaging. Light energy must be delivered at a potential source of fluorescence in order to cause emission of fluorescent light. This is not the case with bioluminescence. Bioluminescence does not make use of any external light source. Bioluminescence signals are self generated by the bioluminescent light source without stimulation from an external energy source. Applicants refer to their previous responses on the differences between fluorescence and bioluminescence.

The Office Action on page 7, states that the "applicant's disclosure indicates bioluminescence and fluorescence are interchangeable (page 6, line 23)." The Applicants' disclosure does not state that the two are interchangeable. The entire paragraph of the cited line is found on page 6, line 18 – page 7, line 2 and reads:

> Some further embodiments may detect and record bioluminescent emissions and/or fluorescent emissions. This image data, along with associated x-ray CT images of the same object, can be used to reconstruct a three-dimensional emission image volume and register the bioluminescent CT image to a corresponding x-ray CT or micro-CT image volume of anatomical and pathological structures. In some such embodiments, the bioluminescent (or fluorescent) reconstruction process can be enhanced through the use of knowledge gained from x-ray CT or other anatomic information gathered by use of other imaging devices including, but not limited to, MRI or ultrasound. As a non-limiting example, emitted photons can be collected from multiple directions in three dimensions with respect to a living animal or any other light emitting structure of interest marked by bioluminescent reporter luciferases or fluorescent sources. In some embodiments, a lung and/or various tumors may be imaged.

(Emphasis added). This paragraph merely states that light received from either a fluorescent or a bioluminescent light source can benefit from information obtained through other imaging means. This does not mean that fluorescence and bioluminescence are interchangeable systems. The independent claims are directed to bioluminescent systems.

At best, the teachings of the present application describe fluorescence as an alternative embodiment. MPEP 2173.05(i) states, "[i]f alternative elements are positively recited in the specification, they may be explicitly excluded in the claims." The present claims are specifically excluding fluorescence. The Office Action on page 7 also states that "bioluminescence does not preclude the addition of external sources." In light of the current amendments, the claims specifically preclude the addition of an external source. Applicants submit that Warren in view of Tomography – Definition from Dictionary.com does not render obvious Applicants'

independent claims 1 or 16. Applicants respectfully request withdrawal of the rejection and allowance of claims 1-11, 13-26, and 28-30 as the cited prior art references do not teach or suggest all the claim limitations.

V. Conclusion

Warren in combination with Tomography-Definition from Dictionary.com does not render obvious any of the pending claims. As the Court noted in *In re Fine*, "dependent claims are nonobvious under section 103 if the independent claims from which they depend are nonobvious." 5 U.S.P.Q.2d 1569, 1600 (Fed. Cir. 1988). Since the Applicants respectfully assert that all the pending independent claims are allowable, all the pending dependent claims are also allowable. Thus, Applicants respectfully request allowance claims 1-11, 13-26, and 28-30 in view of the previous remarks and amendments. The Examiner is invited and encouraged to contact directly the undersigned if such contact may enhance the efficient prosecution of this application to issue.

In light of the remarks above, Applicant respectfully submits that the application is in condition for allowance and respectfully requests that a Notice of Allowance be issued. The Examiner is encouraged to contact Applicant's undersigned attorney to resolve any remaining issues in order to expedite examination of the present application.

Under 37 C.F.R. §1.114, a Request for Continued Examination must be accompanied with a submission. This reply satisfies the requirement of a submission because it is fully responsive.

Enclosed is (1) a Request for Continued Examination, (2) the fee corresponding to the Request for Continued Examination, (3) a Request for a Three-Month Extension of Time, and (4) the fee corresponding to the Request for an Extension of Time. The total payment amount enclosed is $960.00, which represents the $555.00 small entity fee pursuant to 37 C.F.R. § 1.17(a)(3) for a Three-Month Extension of Time and the $405.00 small entity fee pursuant to 37 C.F.R. § 1.17(e) for a Request for Continued Examination. The Commissioner is hereby authorized to apply this fee and any additional fees which may be required, or credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,

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